REMARKS

Reexamination and reconsideration in light of the foregoing proposed amendment and the following remarks is respectfully requested.

Claims 1-23 and 54-56 are pending in this application. Claims 24-53 have been withdrawn from consideration due to a restriction requirement and have been canceled without prejudice, subject to Applicants' right to file a divisional application on the non-elected invention. It is proposed to amend claims 9, 12, 13, 54 and 56. A marked up version of the changes to these claims appears in the Appendix attached hereto. The proposed amendments do not raise any issue of new matter. The amendments are needed to correct obvious errors. Accordingly, the amendments should not require any new consideration and/or search by the Examiner. It is requested that the amendment be given favorable consideration and entered.

In the Office Action Summary, it is noted that the Examiner acknowledged Applicants' claim for foreign priority under 35 U.S.C. § 119 and receipt of the certified copy of the priority document in the National Stage application from the International Bureau.

It is further noted the Examiner's requirement for formal drawings. Drawings are submitted with this response. It is believed that the drawings are now in compliance with the drawing requirements. It is respectfully requested that the Examiner approve the drawings.

REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH

Claims 1-23 and 54-56 stand rejected under 35 U.S.C. § 112, first paragraph, "as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention." In particular, the Examiner is of

the opinion that "claim 1 is directed to a method of selecting a compound, however the specification does not provide basis for selecting a compound as per the steps in the instant claims." The Examiner finds that "the process of selection is described in relation to the identification of compounds of a particular structure as seen in Group II, claims 24-29; versus the design of a compound" and "thus the method of selecting a compound is new subject matter." The Examiner concludes that "the specification does not provide basis for selecting a compound as per the steps in the instant claims." Applicants respectfully traverse this rejection.

The written description requirement under 35 U.S.C. 112, first paragraph, requires that the disclosure, as originally filed, reasonably conveys to one of ordinary skill in the art that the inventor had in his possession the later added limitations to the claimed invention, as of the filing date of the application. *In re Wertheim*, 541 E.2d 257, 262, 191 USPQ 90, 96 (CCPA 1976). All that is required to satisfy the description requirement under 35 U.S.C. 112, first paragraph, is that the originally filed disclosure would have conveyed to one having ordinary skill in the art that an applicant had possession of the concept of what is later claimed. *In re Anderson*, 471 F.2d 1237, 1244, 176 USPQ 331, 336 (CCPA 1973). For reasons set forth below, the claimed method of selecting a compound satisfies the written description requirement of 35 U.S.C. § 112, first paragraph, and does not constitute new subject matter.

The Examiner has not presented any evidence or cogent scientific reasoning to support the conclusion that the term "selecting" constitutes new matter. The Examiner has not explained what "basis" is missing and why such a "basis" is insufficient to establish that a person having ordinary skill in the art would have concluded that the Applicant was not in possession of the concept which is now claimed. The specification on page 5, line 17 describes an embodiment of

the first aspect of the invention which involves "selecting or designing a compound" which has portions that match residues positioned on the surface of the receptor. A person skilled in the art would have understood from the specification that Applicants were in possession of the claimed invention as set forth in claim 1 and the claims dependent thereon, i.e., a compound can be obtained by either designing or *selecting* a compound which binds to a molecule of the EGF receptor family and modulates an activity mediated by the receptor molecule. The detailed description at pages 12-14 of the specification clearly relates to the invention as defined in present claim 1. Page 13, line 16 states that there are two approaches to designing a molecule. The first of these is the "geometric approach". This approach is described in the paragraph bridging pages 13 and 14 and clearly encompasses searching databases and selecting a compound that has a stereochemical structure that is stereochemical complementarity to the EGF receptor molecule. Also at page 14, lines 27-30, the specification refers to programs suitable for "pharmacophore selection and design." The Examiner's attention is also directed to page 5, line 26 of the specification refers to "screening for, or designing, a compound" within the context of the first aspect of the invention. In view of these references to "selecting" suitable compounds it is Applicants' view that the amendment to claim 1 to insert the phrase "or selecting" into the preamble, the amendatory matter does not constitute new subject matter. It is amply supported by the original disclosure.

For the foregoing reasons, it is respectfully requested that the rejection under the first paragraph of 35 U.S.C. § 112, first paragraph, be reconsidered and withdrawn.

REJECTION UNDER 35 U.S.C. § 112, SECOND PARAGRAPH

Claims 1-23 and 54-56 stand rejected under 35 U.S.C. § 112, second paragraph, "as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention." According to the Examiner, the claims are indefinite for the following reasons:

1. The Examiner found claims 1-23 and 54-56 to be "vague and indefinite due to the lack of clarity in the claim language 'designing or selecting' claim 1, line 1." According to the Examiner, the "body of the claim lacks any active steps of design in addition to lacking any steps of selection." Also according to the Examiner, "Applicant may intend step B to represent the step of selection, however obtaining a compound insinuates the completion of selecting one compound" and thus, "it is unclear what steps of methodology applicant looks to define as the active steps of design or selection, aside from the description or characterization of the desired compound."

2. The Examiner found claims 1-23 and 54-56 to be indefinite "for failing to recite a final process step that agrees back with the preamble." According to the Examiner, the "preamble indicates a process of design or selecting." The Examiner made a finding that "if a process of design is intended then the basic steps of ligand or molecular design must be recited in a positive, active fashion" and that if "a process of selection is intended then the active steps of selection by discrimination from a collection of compounds must be present in some manner in order for the following steps of compound assessment to specific criterion to be met." The Examiner refers to claim 1 as an example and states that "claim 1 is drawn to a method for designing a compound that binds to a molecule, yet the claim recites only the characterization of

the molecule to which the binding of the designed compound occurs." The Examiner concludes that the claims "lack an actual step that demonstrates the method of design or selection to produce a successful EGF-receptor binding compound as recited in the preamble; thus do not accomplish that which the preamble sets forth."

3. The Examiner found that claims 1-23, 54 and 56 are "vague and indefinite due to the lack of clarity of the claim language "obtaining a compound" in step (B)" in that it is "unclear if the compound intended is one other than that in the preamble or that in step (A)." 4.

4. The Examiner found claims 1-23 and 54-56 to be "vague and indefinite due to the lack of clarity of the term "obtaining" in step (B)" in that it is "unclear as to what are the metes and bounds of the parameters that define obtaining a compound." According the Examiner, "[i]t is unclear if the compounds are obtained virtually, as by selection from screening a database, or by experimental assays."

5. Finally, the Examiner found claims 2 and 3 to be "vague and indefinite due to the lack of clarity of the term "complement" in that it is "unclear what are the metes and bounds of the parameters that define the degree of complementarity required."

All of these rejections appear to have a common theme. The claims are indefinite because they fail to set forth how the compounds are "designed" or "selected" and that the "degree of complementarity" is not set forth in the claims. In essence, the Examiner is arguing that the claims are unduly broad in scope and that the terms "designing", "selecting", "obtaining" and "stereochemical complementary" would not apprise a person having ordinary skill in the art of the mets and bounds of the claimed subject matter.

To the extent that the Examiner's rejection the claims as indefinite is based on breadth, it is well established that breadth is not indefiniteness. *In re Gardner*, 427 F.2d 786, 788, 166 USPQ 138, 140 (CCPA 1970); *In re Conley*, 490 F.2d 972, 975, 180 USPQ 454, 456 (CCPA 1974). The legal standard for indefiniteness under the second paragraph of 35 U.S.C. § 112 is whether a claim reasonably apprises those of skill in the art of its scope. *See Amgen Inc. v. Chugai Pharmaceutical Co., Ltd.*, 927 F.2d 1200, 1217, 18 USPQ2d 1016, 1030 (Fed. Cir.), *cert. denied sub nom., Genetics Inst., Inc. v. Amgen, Inc.*, 112 S.Ct. 169 (1991). The definiteness of the language employed must be analyzed, not in a vacuum, but always in light of the teachings of the prior art and the application disclosure as it would be interpreted by one possessing the ordinary level of skill in the pertinent art. *See In re Angstadt,* 537 F.2d 498, 501, 190 USPQ 214, 217 (CCPA 1976).

The ordinary meaning of "designing" is to "devise for a specific function or end."[1] The ordinary meaning of "selecting" is to choose from a number or group by fitness or preference.[2] The specification teaches that the invention relates to the field of using the epidermal growth factor (EGF) receptor structure to select and screen for ligands of the EGF receptor. The disclosure at page 4, lines 10-33 and page 5, lines 3-11 and 16-33 states that

> in a first aspect the present invention provides a method of designing a compound which binds to a molecule of the EGF receptor family and modulates an activity mediated by the molecule, which method comprises the step of assessing the stereochemical complementarity between the compound and a topographic region of the molecule, wherein the molecule is characterised by
>
> (i) amino acids 1-621 of the EGF receptor positioned at atomic coordinates substantially as shown in Figure 6;
>
> (ii) one or more subsets of said amino acids related to the coordinates shown in Figure 6 by whole body translations and/or rotations; or

[1] *Webster's Ninth New Collegiate Dictionary, Merriam-Webster, Inc.*, p. 343 (1988).
[2] Ibid, p. 1064.

(iii) amino acids present in the amino acid sequence of a member of the EGF receptor family, which form an equivalent three-dimensional structure to that of the receptor site defined by amino acids 1-621 of the EGF receptor positioned at atomic coordinates substantially as shown in Figure 6.

In a preferred embodiment of the first aspect, the topographic region of the molecule is defined by amino acids 1-475 of the EGF receptor, or an amino acid sequence which forms an equivalent three-dimensional structure to that of the region defined by amino acids 1-475 of the EGF receptor positioned at atomic coordinates substantially as shown in Figure 6.

* * *

The EGF receptor molecule defined in the first aspect of the present invention is depicted in Figure 5. The fragment comprising residues 1-475 of the receptor comprises the L1, S1 and L2 domains of the ectodomain of the EGF receptor. At the centre of this structure is a cavity, bounded by all three domains, of sufficient size to accommodate a ligand molecule.

The fragment comprising residues 313-621 comprises the L2 and S2 domains, which are positioned such that they form a "corner" structure. It is envisaged that this corner structure provides a further binding site for ligands of EGF receptor family members.

* * *

In a preferred embodiment of the first aspect of the present invention, the method further involves selecting or designing a compound which has portions that match residues positioned on the surface of the receptor site as depicted in Figures 7, 8 and 9. By "match" we mean that the identified portions interact with the surface residues, for example, via hydrogen bonding or by enthalpy-reducing Van der Waals interactions which promote desolvation of the biologically active compound within the site, in such a way that retention of the compound within the cavity is favoured energetically.

In a further preferred embodiment of the first aspect of the present invention, the method includes screening for, or designing, a compound which possesses a stereochemistry and/or geometry which allows it to interact with both the L1 and L2 domains of the receptor site. It is believed that EGFR monomers may dimerise in nature in such a manner that the cavities of each monomer may face each other. Accordingly, the method of the first aspect of the present invention may involve screening for, or designing, a biologically active compound which interacts with the Li domain of one monomer and the L2 domain of the other monomer.

It is clear from these passages that the stereospecific structure of the EGF receptor is known and that a three dimensional model structures of the various domains of the EGF receptor are shown in Figs. 7, 8 and 9. In addition, the disclosure at page 7 discloses that the compounds that can bind with the EGF receptor can be determined by using computer modeling and accessing databases of three dimensional chemical structures. The disclosure refers to known computer modeling techniques, databases, and computer software programs at page 13, line 6 to page 15, line 13. The disclosure discusses modeling using the MODELLER program (pages 16 and 17) in addition to a detailed discussion of the domains of the EGF receptor (pages 18-26). With knowledge of the specific structure of the receptor, computer modeling can be used to construct a model or partial model of a ligand that would bind with the receptor (see page 27 of the specification). Clearly, computers can also be used to search three-dimensional databases having known chemical structures to find compatible ligands (see page 14 of the specification). The teachings of the specification are amply corroborated by citations to publications.

The term "obtaining" means to gain or attain usually by planned action or effort.[3] By "designing" a ligand using the receptor as a model or by "selecting" a compound from a three-dimensional database with specific knowledge of the EGF receptor structure, one would have been "obtaining" because the ligand is gained or attained by a planned action.

Thus, a person having ordinary skill in the art reading the specification and knowing the ordinary meaning of the "designing," "selecting," and "obtaining" would have knowledge of the scope or mets and bounds of the claims.

---

[3] Ibid, p. 816.

As for the term "stereochemical complementarity", this term has been defined in the specification at page 5, lines as meaning that "the substance or a portion thereof correlates, in the manner of the classic 'lock-and-key' visualisation of ligand-receptor interaction, with the cavity in the receptor site. A person having ordinary skill in the art would have understood the "degree of complementarity" from the teachings of the application disclosure to mean the classic "lock-and-key" approach. Therefore, such a person would have been apprised of the scope of the claimed invention.

For all of the foregoing reasons, the specification and claims comport with the requirements of the second paragraph of 35 U.S.C. § 112. It is, therefore, respectfully requested that the rejection be reconsidered and withdrawn.

Claims "54 and 46" [sic, 56] stand rejected under 35 U.S.C. § 112, second paragraph, as being "vague and indefinite due to the lack of clarity of the claim language 'the testing in (v)'" since "claim 1 does not have a step (v)." The recitation of step "(v)" is an obvious error and should have been step "(C)". It is proposed to amend claims 54 and 56, accordingly, to correct the error.

Claims 9, 12 and 13 have been objected to because "the term 'sheet' is missing the appropriate symbol "β" as recited in the original claims. The Examiner required correction of the claims. The error occurred due the printer failing to print the beta character. Accordingly, it is proposed to amend the claims to correct the error. The addition of the beta character does not raise an issue of new matter because as pointed out by the Examiner, support for the inclusion of the character can be found in original claims 9, 12 and 13.

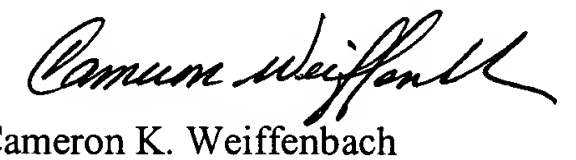
CONCLUSION

For the foregoing reasons, it is submitted that the claims 1-23 and 54-56 comply with the requirements of 35 U.S.C. § 112. Accordingly, favorable reconsideration of the claims is requested in light of the preceding amendments and remarks, and the allowance of the claims is courteously solicited.

To the extent necessary, a petition for an extension of time under 37 C.F.R. 1.136 is hereby made. Please charge any shortage in fees due in connection with the filing of this paper, including extension of time fees, to Deposit Account 500417 and please credit any excess fees to such deposit account.

Respectfully submitted,

McDERMOTT, WILL & EMERY



Cameron K. Weiffenbach
Registration No. 44,488

600 13th Street, N.W.
Washington, DC 20005-3096
(202) 756-8000 CKW:apr
Facsimile: (202) 756-8087
Date: December 17, 2002

APPENDIX

VERSION WITH MARKINGS TO SHOW CHANGES MADE

Please amend claim 9, 12, 13, 54 and 56 as follows:

9. (Three Times Amended) A method as claimed in claim 1, in which the compound is designed or selected to interact with the β-sheet of the L1 domain causing an alteration in the position of the L1 domain relative to the position of the S1 domain or the L2 domain.

12 (Three Times Amended) A method as claimed in claim 1, in which the compound is designed or selected to interact with the β-sheet of the L2 domain causing an alteration in the position of the L2 domain relative to the position of the S2 domain.

13. (Three Times Amended) A method as claimed in claim 1 in which the compound is designed or selected to bind to a lower face containing the second β-sheet of the L1 and/or L2 domains, wherein the structure of the face is characterized by a plurality of solvent-exposed hydrophobic residues.

54. (Amended) A method according to claim 1, wherein the testing in step (C) [(v)] is carried out *in vitro*.

56. (Amended) A method according to claim 1, wherein the testing in step (C) [(v)] is carried out *in vivo*.